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Potentially modifiable determinants of vitamin D status in an older population in the Netherlands: the Hoorn Study[1–3]

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ABSTRACT

Background: Inadequate vitamin D status is common in many populations around the world.

Objective: The aim was to evaluate potentially modifiable determinants of vitamin D status in an older population.

Design: This was a cross-sectional study from a population-based cohort including 538 white Dutch men and women aged 60–87 y. Vitamin D status was assessed by plasma 25-hydroxyvitamin D [25(OH)D] concentrations.

Results: In the winter period, 51% of the subjects had 25(OH)D concentrations <50.0 nmol/L. Greater body fatness and less time spent on outdoor physical activity were associated with worse vitamin D status. Regular use of vitamin D–fortified margarine products [odds ratio (OR) in a comparison of intake of ≥20 g/d with none: 0.41; 95% CI: 0.20, 0.86; *P* for trend < 0.001], fatty fish (OR for servings of ≥2/mo versus none: 0.41; 95% CI: 0.16, 1.04; *P* for trend = 0.01), and vitamin D–containing supplements (OR for ≥ 1/d versus none: 0.33; 95% CI: 0.17, 0.63; *P* for trend < 0.001) were inversely associated with vitamin D inadequacy [25(OH)D <50.0 nmol/L]. We estimated that combined use of margarine products (20 g/d), fatty fish (100 g/wk), and vitamin D supplements (≥1/d) was associated with a 16.8 nmol/L higher 25(OH)D concentration than was the use of none of these. However, none of the participants reached these intakes for all 3 factors.

Conclusion: Because few foods are vitamin D–fortified and the amounts of vitamin D in supplements are low, it is difficult to achieve adequate vitamin D status through increasing intakes in the Netherlands and in countries with similar policies. *Am J Clin Nutr* 2007;85:755–61.

KEY WORDS Vitamin D, food fortification, supplement use, body fatness, population-based study

INTRODUCTION

The importance of vitamin D for bone health and muscle function has long been acknowledged, and accumulating evidence suggests that adequate vitamin D status may contribute to the prevention of autoimmune diseases, hypertension, and various types of cancer (1). Inadequate vitamin D status can be subdivided into "vitamin D insufficiency," characterized by elevated serum parathyroid concentrations and a mild increase in bone turnover, and "vitamin D deficiency," characterized by high bone turnover and possible bone mineralization defects (2). Vitamin D insufficiency is highly prevalent in many populations around the world (3), and vitamin D deficiency is common in institutionalized elderly (2) and Europeans of non-Western origin (4, 5).

Vitamin D is derived from dietary sources or from endogenous production in the skin under the influence of sunlight exposure (6). Possible measures to improve vitamin D status can target consumption of vitamin D–rich foods, fortification of foods, use of dietary supplements, or habits related to sun exposure. Vitamin D fortification of foods varies widely across the world: in the Netherlands, margarine products are the only foods that are vitamin D fortified; in the US and Canada, milk is generally vitamin D fortified; and in many other countries, foods are rarely vitamin D fortified (7). Currently, there is no consensus about the optimal strategy to improve the vitamin D status of populations, and information on the importance of various potentially modifiable determinants of vitamin D status may help to identify promising interventions. Few studies have examined the consumption of various foods in relation to vitamin D status (8, 9), and the effect of vitamin D fortification can be well studied in the Netherlands, because margarine products, but not other foods, are consistently fortified with vitamin D. We therefore examined determinants of vitamin D status in a population-based study of older men and women in the Netherlands, with a focus on dietary factors.

SUBJECTS AND METHODS

Study population

The present study was based on cross-sectional data from white men and women aged 60–87 y who participated in the 2000–2001 Hoorn Study follow-up examination (10). The

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Hoorn Study is a population-based cohort study of glucose metabolism that started in 1989. The baseline examination was conducted in a random sample obtained from the municipal registry of the town of Hoorn, The Netherlands. From January 2000 through July 2001, a follow-up examination was conducted in surviving participants who had given permission to be recontacted. We invited all participants who had type 2 diabetes mellitus, and a random sample of those with impaired and normal glucose metabolism, at the previous follow-up examination in 1996–1998. Of those invited, 648 (60%) participated. The reasons that were given for nonparticipation were lack of interest (30%), morbidity (23%), old age (7%), unwillingness to travel (6%), participation considered too time-consuming (6%), and miscellaneous reasons (15%); 13% did not provide reasons for nonparticipation. After exclusion of persons with clinical type 2 diabetes (n = 67) who may have changed their lifestyle or reporting thereof as a result of the physician diagnosis and persons with missing data for any of the studied variables (n = 43), 538 persons remained for the current analysis. All participants provided written informed consent, and the study was approved by the Ethics Committee of VU University Medical Center Amsterdam.

Measurements

Vitamin D status was assessed by measuring 25-hydroxyvitamin D [25(OH)D] concentrations in fasting EDTA-plasma by using a competitive binding protein assay (DiasSorin, Stillwater, MN). This concentration is considered the most accurate measure of vitamin D status (11). The assay measures both 25-hydroxyvitamin D_2 and 25-hydroxyvitamin D_3, but will primarily represent 25-hydroxyvitamin D_3 concentrations in the current study, because vitamin D in the Dutch diet is mostly vitamin D_3. Laboratory measurements were conducted at the Endocrinology Laboratory, Department of Clinical Chemistry, VU University Medical Center Amsterdam. The interassay CV was 10–15%, with a slightly lower CV at higher concentrations. We performed a whole-body dual-energy X-ray absorptiometry scan using fan beam technology (QDR-2000, software version 7.20D; Hologic, Brussels, Belgium) to assess the percentage of body fat (10). Cigarette smoking habits and education level were assessed by self-administered questionnaires. High education level was defined as vocational colleges and university, medium level as secondary education, and low level as elementary school, lower vocational training, or less. Usual food consumption and supplement use and physical activity, including commuting activities, leisure time activities, and occupational activities, were assessed by using validated questionnaires (12, 13). Vitamin D–containing supplements included vitamin A and D supplements, calcium and vitamin D supplements, and multivitamins, which were the most commonly used vitamin D–containing supplements in the Netherlands. Dairy was considered to be high-fat if it contained >2% of weight as fat. "Fatty fish" included, for example, eel, mackerel, and herring, whereas "lean fish" included cod, plaice, mussels, and shrimp. Time spent on outdoor physical activity was estimated by adding the time spent on walking, cycling, and gardening.

Statistical analysis

Vitamin D status was categorized by using previously defined cutoffs (2). Although higher cutoffs have been proposed (1), we defined "vitamin D inadequacy" as 25(OH)D concentrations <50 nmol/L for the purpose of the current analysis. Statistical analyses were conducted by using SAS software version 8.2 (SAS Institute, Cary, NC). Differences by sex and season were evaluated by using Student's t test for continuous variables, the Wilcoxon's rank-sum test for continuous variables that were not normally distributed, and a chi-square test for categorical variables. We performed linear regression analysis to derive regression coefficients for analyses with 25(OH)D concentrations as the dependent variable and logistic regression analysis to derive odds ratios for analyses with vitamin D inadequacy as the dependent variable. To address potential confounding by other determinants of vitamin D status, we used a multivariable model that included age (y), sex (man or woman), body fat (percentage), cigarette smoking (current, past, or never), education level (high, medium, or low), use of vitamin D–containing supplements (none, <1/d, or ≥1/d), outdoor activities (h/d), season (December to February, March to May, June to August, or September to November), total energy intake (kJ/d), and consumption (servings/d) of margarine products, eggs, fatty fish, lean fish, red meat, poultry, high-fat dairy, and low-fat dairy. Analysis of covariance was used to obtain mean 25(OH)D concentrations with adjustment for age, sex, and season according to tertiles of body fatness. P values for interaction were obtained by adding a multiplicative interaction term to the regression model. All reported P values were two-sided, and P values < 0.05 were considered statistically significant.

RESULTS

The characteristics of the study population are shown in **Table 1**. Approximately 50% of the population were women, and the mean (±SD) age was 69.6 ± 6.5 y. In the winter period, 51% had a 25(OH)D concentration <50.0 nmol/L compared with 34% in the summer period (**Table 2**).

Determinants of 25-hydroxyvitamin D concentrations

After multivariable adjustment, older age, higher educational level, and higher body fatness were significantly associated with worse vitamin D status (**Table 3**). More time spent on outdoor activities, use of vitamin D–containing supplements, and consumption of margarine products (vitamin D fortified in the Netherlands), fatty fish, and red meat were associated with better vitamin D status. In contrast, cigarette smoking, and consumption of dairy products (not fortified), eggs, lean fish, and poultry were not substantially associated with vitamin D status. When calcium intake was included in the multivariable model instead of dairy products, it was not associated with higher 25(OH)D concentrations either [$\bar{x}$ (±SE) calcium intake: −0.32 ± 0.24 nmol/L per 100 mg/d increment; P = 0.18).

Sex differences in vitamin D status

After adjustment for only age and season, women had a 6.0 ± 1.5 nmol/L lower 25(OH)D concentration than did the men (Table 3). After adjustment for percentage body fat, this association disappeared (women compared with men: −0.2 ± 2.2 nmol/L), which suggests that the greater body fatness of women explains the sex difference in vitamin D status. As additionally indicated in **Figure 1**, the vitamin D status of men and women did not differ significantly at the same body fat percentage. The association between body fatness and vitamin D status did not differ substantially by sex (P for interaction = 0.38).

TABLE 1
Characteristics of the study population

	Men (n = 271)	Women (n = 267)	P[1]
Age (y)	69.4 ± 6.3[2]	69.8 ± 6.7	0.43
Percentage body fat (%)	27.6 ± 6.5	41.5 ± 6.7	<0.0001
Current cigarette smoker [n (%)]	55 (20.3)	31 (11.6)	0.006
Low education level [n (%)][3]	117 (43.2)	140 (52.4)	0.03
Daily use of supplements with vitamin D [n (%)]	27 (10.0)	42 (15.7)	0.05
Outdoor activities (h/d)	0.9 (0.3–1.8)[4]	0.7 (0.3–1.3)	0.03
Dietary intake			
Margarine products (g/d)	17.4 (7.1–26.0)	10.7 (4.5–17.4)	<0.0001
Eggs (g/d)	14.3 (7.1–21.4)	14.3 (6.7–21.4)	0.17
Fatty fish (g/d)	2.2 (0.9–4.7)	1.4 (0.3–4.7)	0.006
Lean fish (g/d)	7.3 (2.2–13.4)	6.1 (1.2–12.3)	0.08
Red meat (g/d)	49.4 (31.8–70.9)	34.1 (19.1–54.5)	<0.0001
Poultry (g/d)	6.9 (3.1–16.0)	6.3 (1.6–12.9)	0.03
High-fat dairy (servings/d)	4.0 (3.1–5.7)	3.9 (2.9–5.4)	0.10
Low-fat dairy (servings/d)[5]	1.5 (0.8–2.5)	1.8 (1.1–2.9)	0.002
Calcium (mg/d)	1054 ± 366	1065 ± 350	0.74

[1] Differences by sex were evaluated by using Student's t test for continuous variables, the Wilcoxon rank-sum test for continuous variables that were not normally distributed, and a chi-square test for categorical variables.
[2] $\bar{x}$ ± SD (all such values).
[3] Low level denotes elementary school, lower vocational training, or less.
[4] Median; interquartile range in parentheses (all such values).
[5] Serving sizes were 10 g for butter and cheese and 150 g for fluid dairy products.

Margarine, fatty fish, and supplement use in relation to vitamin D inadequacy

Because consumption of foods and use of supplements are often considered as targets for interventions to achieve adequate vitamin D status in populations, we further examined these factors in relation to vitamin D inadequacy. On the basis of the strength of the associations with plasma 25(OH)D concentrations, we limited this analysis to the use of margarine products, fatty fish, and vitamin D–containing supplements. All these factors were inversely associated with vitamin D inadequacy (**Table 4**). However, the prevalence of vitamin D inadequacy was still substantial for participants with favorable levels for these exposures (Table 4). We also examined combinations of margarine, fish, and supplement use. No suggestions of interactions were observed between margarine, fatty fish, and supplement use in relation to 25(OH)D concentrations or prevalence of vitamin D inadequacy (all P values for interaction > 0.40). From the multivariable-adjusted regression coefficients, we estimated that the combined use of 20 g margarine products/d, ≥1 vitamin D–containing supplement/d, and 100 g fatty fish/wk (a total intake of ≈6.4 μg/d vitamin D; **Table 5**) was associated with a 16.8 nmol/L higher 25(OH)D concentration and an odds ratio of vitamin D inadequacy of 0.07. However, none of the participants reached these intakes for all 3 factors.

TABLE 2
Vitamin D status of the study population based on plasma 25-hydroxyvitamin D [25(OH)D] concentrations in 538 Dutch men and women aged 60–87 y[1]

	Summer months (n = 172)	Winter months (n = 366)
25(OH)D concentration (nmol/L)	61.3 ± 20.1[2]	50.5 ± 18.3[3]
25(OH)D percentiles (nmol/L)		
5th	30.4	23.8
25th	45.5	35.3
50th	62.1	49.0
75th	73.5	64.0
95th	99.2	84.1
25(OH)D categories [n (%)]		
<25.0 nmol/L	3 (1.7)	24 (6.6)
25.0–49.9 nmol/L	55 (32.0)	162 (44.3)
50.0–74.9 nmol/L	73 (42.4)	143 (39.1)
≥75.0 nmol/L	41 (23.8)	37 (10.1)[3]

[1] Summer months: June through November; winter months: December through May.
[2] $\bar{x}$ ± SD (all such values).
[3] Significantly different from summer months, $P < 0.001$ (Student's t test for continuous variables and chi-square test for categorical variables).

DISCUSSION

In our population-based study of older white men and women in the Netherlands, lower body fatness, more time spent on outdoor physical activity, and use of fortified margarine products, fatty fish, and vitamin D–containing supplements were associated with better vitamin D status. Individually, however, regular use of vitamin D–containing supplements, fatty fish, and fortified margarine were not sufficient to achieve adequate vitamin D status.

Older age and female sex were associated with substantially worse vitamin D status, which agrees with results from earlier studies (8, 15, 16). Our data suggests that the sex difference in vitamin D status may be due to the generally higher body fatness observed in women than in men. An inverse association between body fatness and vitamin D status has been reported previously (16–18) and may reflect excess vitamin D storage in adipose

TABLE 3
The association between dietary and other potential predictors of vitamin D status and plasma 25-hydroxyvitamin D [25(OH)D] concentrations in 538 Dutch men and women aged 60–87 y

		Difference in 25(OH)D (nmol/L)			
		Adjusted for age, sex, and season[1]		Adjusted for other predictors[2]	
Predictor	Increment	RC (SE)[3]	*P*	RC (SE)[3]	*P*
Age	10 y	−9.5 (1.2)	<0.001	−8.3 (1.2)	<0.001
Sex	Female vs male	−6.0 (1.5)	<0.001	3.2 (2.3)	0.16
Body fat	10%	−4.2 (0.1)	<0.001	−4.6 (1.2)	<0.001
Cigarette smoker	Current vs never	−0.6 (2.3)	0.80	−3.5 (2.3)	0.12
Education level[4]	Medium vs low	−2.7 (1.6)	0.10	−3.5 (1.6)	0.03
	High vs low	−6.5 (2.5)	0.009	−7.7 (2.4)	0.002
Supplements with vitamin D	Daily use vs no use	6.4 (2.3)	0.005	7.8 (2.2)	<0.001
Outdoor activities	1 h/d	1.8 (0.6)	0.003	1.8 (0.6)	0.002
Food consumption					
Margarine products	1 serving/d	2.5 (0.7)	<0.001	2.1 (0.7)	0.001
Eggs	1 serving/d	−0.4 (2.9)	0.89	−0.9 (2.8)	0.74
Fatty fish	1 serving/wk	2.6 (1.9)	0.16	4.8 (2.2)	0.03
Lean fish	1 serving/wk	0.2 (1.0)	0.81	−0.9 (1.2)	0.47
Red meat	1 serving/wk	0.3 (0.2)	0.20	0.5 (0.2)	0.05
Poultry	1 serving/wk	−0.2 (0.7)	0.81	0.4 (0.7)	0.62
High-fat dairy	1 serving/d	−0.4 (0.3)	0.22	−0.2 (0.3)	0.57
Low-fat dairy	1 serving/d	−0.4 (0.5)	0.42	−0.9 (0.5)	0.09

[1] Adjusted for age (y), sex, and season (December through February, March through May, June through August, or September through November) by using multivariable linear regression analysis. Additional adjustment for total energy intake (kJ/d) was performed for the models with food variables.

[2] The multivariable model included age, sex, season, total energy intake, body fat (%), cigarette smoking (current, past, or never), education level (high, medium, or low), use of vitamin D–containing supplements (none, <1/d, or ≥1/d), outdoor activities (h/d), and consumption (servings/d) of margarine products, eggs, fatty fish, lean fish, red meat, poultry, high-fat dairy, and low-fat dairy.

[3] Regression coefficient (RC) reflecting the difference in 25(OH)D (nmol/L) for each given increment in the exposure variable. Serving sizes were 10 g for margarine, butter, and cheese; 150 g for fluid dairy products; 100 g for red meat, poultry, and fish; and 50 g for eggs.

[4] High level includes vocational college or university, medium level includes secondary education, and low level includes elementary school, lower vocational training, or less.

tissue (19). It was also suggested that poor vitamin D status may increase adiposity through increased lipogenesis as a result of elevated parathyroid hormone concentrations (17).

Consistent with previous studies, regular use of fatty fish (8, 9) or vitamin D–containing supplements (11, 15, 20, 21) were associated with substantially better vitamin D status than was no

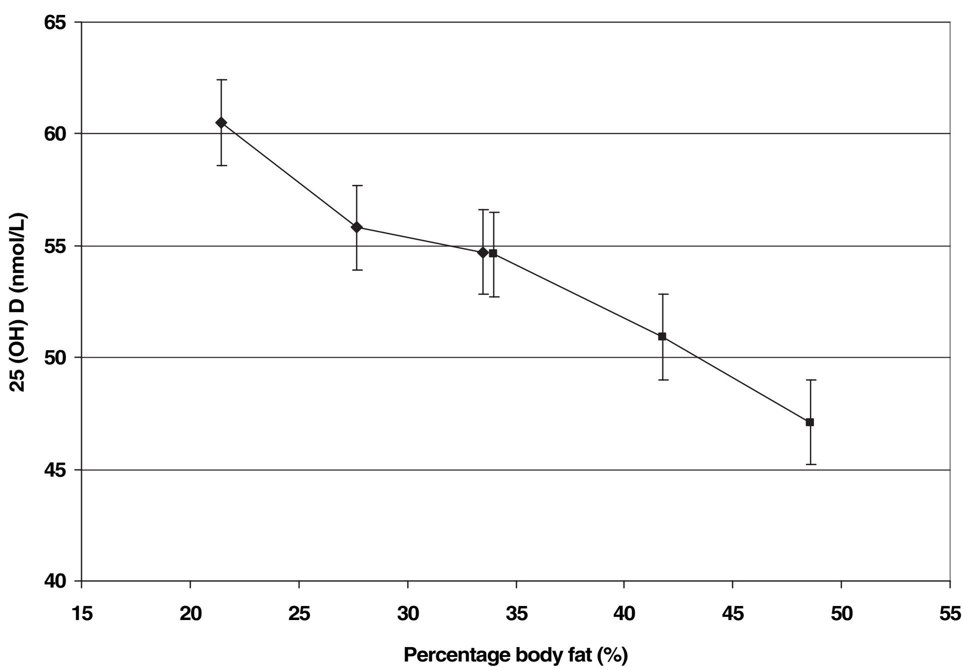

FIGURE 1. Mean (±SE) plasma 25-hydroxyvitamin D [25(OH)D] concentrations according to sex-specific tertiles of percentage body fat in 538 Dutch men (◆) and women (■) aged 60–87 y. Data were adjusted for age, season, and educational level by using ANCOVA.

TABLE 4
Odds ratios (ORs) for vitamin D inadequacy for the use of margarine products, fatty fish, and supplements in 538 Dutch men and women aged 60–87 y[1]

Categories of exposure	*n*	25(OH)D <50.0 nmol/L	OR (95% CI)[2]	*P* for trend[3]
		n (%)		
Margarine				
No use	59	34 (58)	1 (ref)	
<10 g/d	155	89 (57)	0.83 (0.40, 1.74)	
10–19.9 g/d	163	70 (43)	0.55 (0.27, 1.14)	
≥20 g/d	161	51 (32)	0.41 (0.20, 0.86)	<0.001
Fatty fish				
No use	69	43 (62)	1 (ref)	
<1.0 serving/mo	287	130 (46)	0.66 (0.34, 1.30)	
1.0–1.9 servings/mo	102	38 (38)	0.47 (0.21, 1.04)	
≥2.0 servings/mo	86	33 (38)	0.41 (0.16, 1.04)	0.01
Vitamin D–containing supplements				
No use	460	220 (48)	1 (ref)	
<1/d	9	2 (22)	0.55 (0.09, 3.33)	
≥1/d	69	22 (32)	0.33 (0.17, 0.63)	<0.001

[1] Vitamin D inadequacy was defined as a plasma 25-hydroxyvitamin D [25(OH)D] concentration <50 nmol/L.
[2] Multivariate-adjusted (as described in the footnotes to Table 2) by using logistic regression analysis.
[3] Calculated by modeling the exposures as continuous variables.

use of these products. Except for fatty fish, however, other foods with naturally occurring vitamin D contributed little to vitamin D status, consistent with their low vitamin D content (Table 5). Consumption of vitamin D–fortified margarine was associated with better vitamin D status in our study, whereas consumption of dairy products that are not fortified in the Netherlands was not. Similarly, intake of calcium from vitamin D–fortified, but not from nonfortified, sources was associated with substantially better vitamin D status in a study conducted in the United States (22). A high calcium intake may have a vitamin D–sparing effect because of a decrease in serum parathyroid hormone and decreased turnover of vitamin D metabolites (2), but this effect may be less relevant in populations with a high calcium intake such as our study population (average intake: 1054 mg/d for men and 1065 mg/d for women). A longitudinal study conducted in young Finnish men suggested that fortification of milk and margarine with vitamin D reduced the prevalence of vitamin D inadequacy by 50%, also underscoring the importance of appropriate vitamin D fortification (23). The Dutch Commodities Act does not allow the addition of vitamin D to foods other than margarine products, with the exception of small amounts for restoration or for substitution products (Table 5). However, in 2004 the European Court of Justice ruled that the Netherlands cannot generally prohibit the addition of vitamin D to foods but has to consider applications for the addition of vitamin D on a case-by-case basis. Studies conducted in the Netherlands and the United Kingdom have shown a much higher prevalence of vitamin D deficiency in persons of non-Western origin than in other residents (4, 5). Because margarine products are less likely to be used (24) and lactose intolerance is more prevalent in these high-risk groups, fortification of foods other than margarine and milk with vitamin D is preferable.

Policies to increase food fortification and allow supplements with larger amounts of vitamin D should consider the risk of

TABLE 5
Vitamin D content of selected Dutch foods and supplements[1]

Food	Serving size	Concentration vitamin D (per serving)	Comments
Supplements	1	≤5.0 μg	Amount allowed per daily dose (typically 2.5 or 5.0 μg per supplement)
Supplements for "at-risk groups"	1	≤15.0 μg	Label should target children aged <6 y or pregnant or lactating women. Since 2005, also allowed for persons aged ≥60 y[2]
Margarine, half-fat	10 g	0.72 μg	Fortified as agreed in a covenant between government and industry with a maximum of 0.075 μg/g[3]
Butter	10 g	0.12 μg	Not fortified
Full-fat milk	150 mL	0.15 μg	Not fortified
Reduced-fat milk (2%)	150 mL	0.00 μg	Not fortified
Mackerel, smoked	100 g	8.0 μg	Not fortified
Salmon, microwave-cooked	100 g	8.7 μg	Not fortified

[1] Values for the foods were calculated from data in reference 14.
[2] Dutch Commodities Act Regulation Exemption for vitamin preparations.
[3] If the label explicitly targets persons aged ≥60 y, fortification of 0.20–0.25 μg/g margarine product is allowed since 2003 (Dutch Commodities Act Regulation Exemption for vitamin D), but this type of margarine does not seem to be commonly available.

vitamin D toxicity (25). Vitamin D intoxication can lead to hypercalcaemia, hypercalciuria, bone resorption, bone loss, and impairment of renal function (2). However, hypercalcaemia due to effects of vitamin D intoxication per se has only been observed for 25(OH)D concentrations >220 nmol/L (25), whereas the 95th percentile concentration observed in our study population for the summer period was 99 nmol/L. This suggests that vitamin D intakes can be substantially higher before toxicity becomes a concern and that risk of vitamin D intoxication is negligible with regular fortification policies (eg 10 μg of vitamin D/L milk or orange juice) (25).

The associations of season and outdoor physical activity with vitamin D status are consistent with the importance of cutaneous vitamin D production under the influence of sunlight. Previous studies have also linked a tendency to stay indoors (8, 15) and wearing long sleeved clothing in sunshine (8) to poor vitamin D status. Although excessive exposure to sunlight increases the risk of skin cancer, sensible sun exposure without getting burned (usually 5–10 min of exposure of the arms and legs or of the hands, arms, and face 2 or 3 times/wk) may be prudent for improving vitamin D status (6). However, for many populations, it seems unlikely that increased sun exposure is a sufficient remedy for inadequate vitamin D status. Poor vitamin D status is observed in countries with abundant sunlight (3), and at the latitude of the Netherlands (≈52 °N) solar radiation is sufficient for vitamin D formation in only 6 mo of the year (26). Therefore, adequate vitamin D stores have to be built up in the summer to prevent vitamin D deficiency in the winter, but in practice, this usually is not sufficient. Also, for the elderly and persons with modest dress (that leaves little of the skin uncovered) because of religious or cultural reasons, it can be difficult to increase sun exposure sufficiently to reach an adequate vitamin D status (24).

Although the direction of effects cannot be determined in cross-sectional studies, an effect of vitamin D status on lifestyle factors does not seem plausible, because the participants were unlikely to be aware of their vitamin D status. Because our study was not a randomized trial, we cannot exclude the possibility of confounding by imperfectly measured or unmeasured factors. In addition, assessment of lifestyle factors by using self-reports has undoubtedly led to some measurement error and a reduced ability to detect associations for contributors of small amounts of vitamin D. The observed associations are generally consistent, however, with data from intervention studies (3, 25) and the vitamin D content of foods and supplements (Table 5).

Our findings suggest that increased adiposity and a sedentary lifestyle, which result in less participation in outdoor activities, may contribute to poor vitamin D status. Because few foods are vitamin D fortified and amounts of vitamin D in supplements are low, it is difficult to achieve adequate vitamin D status through increasing intakes in the Netherlands and countries with similar policies. Use of supplements with higher vitamin D doses would be an effective measure for specific high-risk groups, but the experience from campaigns recommending folate supplements suggest that this strategy may not be effective for large parts of the general population (27). Our results indicate that fortification of margarine with vitamin D substantially contributes to better vitamin D status in the Netherlands and that fortification of other widely used foods, such as milk, yogurt, orange juice (28), and cereal products (29), should be considered.

RMvD conceived the research question, conducted the statistical data analysis, and drafted the manuscript. MBS, JMD, CDAS, LMB, and RJH were involved in the data collection. All authors advised on interpretation of the results, revised the paper critically, and approved the final manuscript. PL received funds for research, fees for consulting, or both from Nycomed, Lilly, MSD, Wyeth, Servier, Aventis, and Procter & Gamble. None of the other authors had a personal or financial conflict of interest.

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